AMENDMENTS TO THE SPECIFICATION:

On page 3, amend the paragraph at lines 4-29 as follows:

In one aspect, the invention provides a modified peptide which has anti-bacterial or anti-fungal activity, and has the formula ~~[SEQ ID NO: 1]~~:
R^1 -Asp-Lys-Gly-X-Y-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-X'-Y'-R^2 (R^1 - SEQ ID NO: 1- R^2),

wherein R^1 is a moiety having a net positive charge;

wherein R^2 is selected from the group consisting of a free hydroxyl, an amide, an imide, a sugar and a sequence of one or up to about 15 additional amino acids, optionally substituted with a free hydroxyl, an amide, an imide or a sugar. These additional amino acids are independently selected from L-configuration or D-configuration. These additional amino acids may be capable of forming a cyclic peptide by linkage to the N-terminal amino acid. Such an amino acid may be modified by the insertion of a sugar, imide groups and the like. These additional amino acids may also form spacers to cyclize the peptide by bridging between the N- and C- termini of the peptide;

wherein X and Y form a dipeptide, which is Ser-Tyr or is a dipeptide formed of naturally occurring amino acids or unnatural amino acids, the dipeptide being resistant to cleavage by endopeptidases; and wherein X' and Y' form a dipeptide, which is Asn-Arg, or is a dipeptide formed of naturally occurring amino acids or unnatural amino acids, the dipeptide being resistant to cleavage by endopeptidases~~, each~~. In one preferred embodiment, this peptide is a cyclic peptide in which R^1 and/or R^2 form an amino acid spacer (which is preferably a sequence duplicating at least a portion of the pyrrhocoricin peptide) linking the N- and C- terminal amino acids of the above formula. The peptides of this formula include modified peptides in which one or more conventional amide bonds between amino acids is replaced with a bond resistant to a protease, such as a thio-amide bond or a reduced amide bond. Further a variety of multimeric peptide constructs are included in this invention.

On page 5, amend the paragraph at lines 2-8 as follows:

Fig. 1 is a graph illustrating the degradation of de-glycosylated pyrrhocoricin (Peptide #1) and a modified pyrrhocoricin peptide of this invention, i.e., 1-aminocyclo-hexane carboxylic acid (Chex)-Pyrrhocoricin- β-acetyl-2,3-diamino propionic ~~acid~~ amide [Dap(Ac)] (Peptide #21) in 25% mammalian sera over time. The different symbols illustrate the pyrrhocoricin or modified peptide in mouse sera (m), in year-old human sera (h1) and in the month-old human sera (h2). The modified peptide is described in detail below in Example 1. The degradation assay is described below in Example 4.

On page 8, line 29 through page 9, line 13, amend the paragraph as follows:

The R^2 group of peptides of the above formula may be a free hydroxyl, an amide, an imide, a sugar, or a sequence of one or up to about 15 additional amino acids, optionally substituted with a free hydroxyl, an amide, an imide or a sugar. The amino acids may be naturally occurring amino acids or unnatural amino acids, such as D configuration amino acids. The additional amino acids may be capable of forming a cyclic peptide by attaching to an amino terminal amino acid. These amino acids may also be modified by insertion of a sugar, imide groups and the like. These additional amino acids may also form spacers, as described above for R^1, to cyclize the peptide by bridging between the N- and C- termini of the peptide. A variety of methods for producing non-natural amino acids are known and may be selected by one of skill in the art. For example, in some peptides, R^2 is D-Asn, L-Asn, Asp, or Asn-R^3, wherein R^3 is a sugar. In some embodiments R^3 is 2-acetamido-2-deoxyglucose; in other preferred embodiments, the R^3 is triacetyl 2-acetamido-2-deoxyglucose. In other embodiments of the peptides of this invention R^2 is a β-acetyl-2,3-diamino propionic ~~acid~~ amide group (DAP(Ac)).

On page 25, lines 1-8 , amend the paragraph as follows:

Active, modified Peptide 9 has a positively charged N-terminal acetyl-Lysine and a β-acetyl-2,3-diamino propionic ~~acid~~ amide group (DapAc) in the L configuration attached to the 19th amino acid residue with the 20th amino acid residue eliminated. The sequence is:
Acetyl-Lys-Val-Asp-Lys-Gly-Ser-Tyr-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-Asn-Arg-***NH-CH-CONH$_2$*** [SEQ ID NO: 13].

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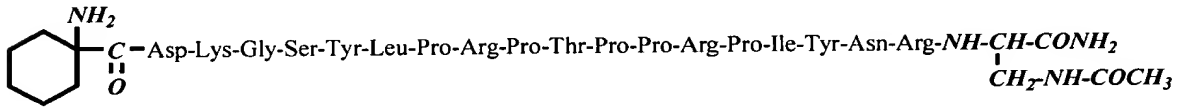
CH$_2$-NH-COCH$_3$.

On page 27, lines 15 to page 28, line 1 , amend the paragraph as follows:

Active, modified Peptide 21 has an R^1 group of 1-aminocyclo-hexane carboxylic acid, and having attached at the C-terminus in place of the 19th amino acid Asn, a β-acetyl-2,3-diamino propionic ~~acid~~ amide group in the L configuration. The sequence is:



[SEQ ID NO: 22].

On page 28, lines 2-8, amend the paragraph as follows:

The active, modified Peptide 22 has an Acetyl-Arg group attached to the N-terminal Val, and having attached at the C-terminus in place of the 20th amino acid Asn, a β-acetyl-2,3-diamino propionic ~~acid~~ amide group in the L configuration. The sequence is:

Acetyl-Arg-Val-Asp-Lys-Gly-Ser-Tyr-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-Asn-Arg-***NH-CH-CONH$_2$*** [SEQ ID NO:23].

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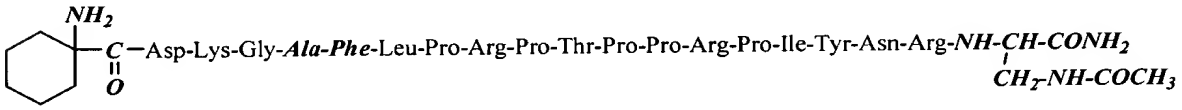
CH$_2$-NH-COCH$_3$

On page 28, lines 10-19, amend the paragraphs as follows:

Inactive Peptide 23 has the R^1 group 1-aminocyclo-hexane carboxylic acid, and replaces Ser5 and Tyr6 with Ala5 and Phe6. Attached at the C-terminus in place of the 19th amino acid Asn is a β-acetyl-2,3-diamino propionic ~~acid~~ amide group in the L configuration. The sequence is [SEQ ID NO:24]:



Active Peptide 24 has attached at the C-terminus in place of the 20th amino acid Asn, a β-acetyl-2,3-diamino propionic ~~acid~~ amide group in the L configuration: Val-Asp-Lys-Gly-Ser-Tyr-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-Asn-Arg-***NH-CH-CONH$_2$*** [SEQ ID NO:25].

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CH$_2$-NH-COCH$_3$.

On page 31, lines 10-25, amend the paragraph as follows:

The results in Table 1 demonstrate several additional characteristics of the modified peptides of this invention vs. the unmodified Peptides 1 and 2 [SEQ ID NO: 6 and 2, respectively]. The differences in the IC_{50} values between the results for Peptide 22 [SEQ ID NO: 23] in two performances of the assay (at time a and 3 months later at time b) demonstrate the variability of the assays. In general, modifications at either termini

reduced the potency of unmodified pyrrhocoricin. From the N- or C-terminally modified peptides, the modifications of a 1-aminocyclo-hexane carboxylic acid at the amino terminus and a β-acetyl-2,3-diamino propionic ~~acid~~ amide group at the carboxy-terminus retained most of the anti-bacterial activity. In a preferred embodiment for drug development, both termini are modified to block or at least retard exopeptidase cleavage. Peptides containing modifications at both termini featured acetylation together with positively charged amino acid addition, incorporation of unnatural amino acids, such as Chex or Dap(Ac), glycosylation, imide formation, D-amino acid substitution or cyclization. Examples of desirable peptides having modifications at both termini are Peptides # 8, 9, 10, 11, 12, 13, 16, 17, 21, and 22 [SEQ ID NOS: 12-16, 26, 17, 18, 22 and 23, respectively].

On page 35, lines 12-24, amend the paragraph as follows:

The degradation products of the modified peptides of this invention (Peptides 1, 21 and 22 [SEQ ID NOS: 6, 22 and 23, respectively]) after a 45-minute digestion with 25% mammalian sera are reported in Table 4. The missing residues are indicated (e.g - C2 means that the C-terminal two residues are cleaved off). For Peptide 22 (which is a modified pyrrhocoricin, having an acetyl-Arg group attached to the N-terminal Val, and having attached at the C-terminus in place of the 20th amino acid Asn, a β-acetyl-2,3-diamino propionic ~~acid~~ amide group in the L configuration), the N-terminal residue numbers correspond to unmodified pyrrhocoricin. In Table 4, the relative amounts of the degradation products are estimated based on the MALDI-MS peak heights. 0=not detected; 1=very weak (below 5000), 2=weak (5-10000), 3=medium (10-15000), 4=strong (15000-uncleaved molecular ion at 25-30000), 5=very strong (above uncleaved molecular ion). All identified degradation products are listed.

On page 36, lines 8-21, amend the paragraph as follows:

When looking at the first metabolites after 45 minute digestion, it is evident that the C-terminal asparagine is cleaved off Peptide 1 [SEQ ID NO: 6]. In contrast, the modified C-terminal residue stays on the peptides containing β-acetyl-2,3-diamino propionic ~~acid~~ amide residues (Peptides 21 and 22) [SEQ ID NOS: 22 and 23, respectively]. The acetyl-Arg amino terminal modified Peptide 22 produces more N-terminal cleavage products close to the amino terminus than Peptide 21 (which is a modified pyrrhocoricin, having in place of the N-terminal Val, the group 1-aminocyclo-hexane carboxylic acid-, and having attached at the C-terminus in place of the 20th amino acid Asn, a β-acetyl-2,3-diamino propionic ~~acid~~ amide group in the L configuration). Most notably, Peptide 21 produces a fragment in which the Val-Asp-Lys tripeptide is missing. While for Peptide 1 the degradation products are different in the two human sera, for Peptide 21, they are very similar. They are also similar to those observed after digestion with the mouse serum. Apparently, Peptide 21, is generally more resistant than Peptide 1 in human serum.

On page 37, lines 1-21, amend the paragraph as follows:

Fig. 1 shows the kinetics of the degradation of Peptides 1 and 21 [SEQ ID NOS: 6 and 22, respectively] in this assay. The curves are fitted to an exponential equation. The degradation curves for Peptide 1 and Peptide 21 (the modified pyrrhocoricin, having in place of the N-terminal Val, the group 1-aminocyclo-hexane carboxylic acid-, and having attached at the C-terminus in place of the 20th amino acid Asn, a β-acetyl-2,3-diamino propionic ~~acid~~ amide group in the L configuration) were similar. Nonglycosylated pyrrhocoricin is somewhat more stable in mouse serum and in the weaker human serum, but much less stable in the more active human serum. Although the lack of endopeptidase cleavage sites reduced the degradation rate of Peptide 21 compared to Peptide 1, this loss of protease activity was compensated for increased exopeptidase activity C-terminal to Ser5 and Asn18. Preliminary metabolism studies of the cyclic Peptide 17 [SEQ ID NO: 18] indicated an endopeptidase cleavage site between Asn18

and Arg19 in human sera. In accordance with the increased number and amount of N-terminal degradation products, Peptide 22 [SEQ ID NO: 23] (a modified pyrrhocoricin, having an acetyl-Arg group attached to the N-terminal Val, and having attached at the C-terminus in place of the 20th amino acid Asn, a β-acetyl-2,3-diamino propionic ~~acid~~ amide group in the L configuration), degrades considerably faster than either Peptide 1 or Peptide 21 (not shown). Remarkably, after 8 hours of digestion, in mouse serum, both Peptides 1 and 21 have 20% of the initial amounts intact. Significantly, after the same period of time, traces of Peptide 21 are still present in all sera studied.